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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,845	10/18/2001	Samy Ashkar	CMCC 779	7069

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EXAMINER	
DEBERRY, REGINA M	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 02/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,845	ASHKAR ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Status of Application, Amendments and/or Claims

The amendment filed 21 November 2003 has been entered in full. Claims 7-18 were cancelled. Claims 1-6 are pending.

The Examiner has acknowledged that cancellation of non-elected species is not, as yet, required. This is in reference to the objection of claim 1, set forth at page 2 of the previous Office Action, 21 August 2003.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The objection of claim 6 under 37 CFR 1.76(c), as being of improper dependent form for failing to limit the subject matter of the previous claim as set forth at page 3 of the previous Office Action (21 August 2003) is *withdrawn* in view of Applicants' arguments (21 November 2003).

The rejection of claim 2 under 112, second paragraph as set forth at page 3 of the previous Office Action (21 August 2003) is *withdrawn* in view of the amendment, (21 November 2003).

The rejection of claims 1-6 under 35 U.S.C. 102(b) as being anticipated by Young *et al.*, Genomics, 1990 as set forth at page 6 of the previous Office Action (21 August 2003) is *withdrawn* in view of the amendment, (21 November 2003).

Specification

The amendment filed 21 November 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "wherein the peptide is not full length human osteopontin" (claim 1).

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112, first paragraph, written description

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.** The specification as originally filed does not provide support for the invention as now claimed: "wherein the peptide sequence is not full length human osteopontin" (claim 1). In addition, the recitation of "not full length human osteopontin" appears to be a negative limitation. Adding the expressed exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded. This clearly illustrates that such negative limitations do, in fact, introduce new concepts. See Ex parte Grasselli, 231 USPQ 393 (BPAI 1983).

Applicants' amendment, filed 21 November 2003 does not provide sufficient direction for the written description for the above-mentioned "limitations". The instant

claims now recite limitations which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as-filed. Applicant is required to cancel the new matter in the response to this Office action. Alternatively, Applicant is invited to provide sufficient written support for the "limitations" indicated above or rely upon the limitations set forth in the specification as filed.

Claim Rejections - 35 USC § 112, first paragraph, scope of enablement

Claims 1-6 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an osteopontin-derived peptide *consisting* of the amino acid of SEQ ID NO:11 wherein the peptide increases cell attachment of osteoprogenitor cells to a biomaterial and increases cell spread of *osteoprogenitor cells,* does not reasonably provide enablement for an osteopontin-derived peptide *comprising* the amino acid of SEQ ID NO:11 which binds *any integrin receptors* on the surface on *any cell type.*

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The basis for this rejection is set forth at pages 3-5 of the previous Office Action (21 August 2003).

Applicants state that Example 12 of the originally filed application illustrates the ease in which one of ordinary skill in the art may identify peptides exhibiting the claimed activities and Table 8 illustrates that antibodies to different integrins may be used to block binding to specific integrins. Applicants states that it should be noted that peptide

size is not critical to binding since the peptide is able to bind when present in the intact full length peptide. Applicants argue that one of ordinary skill in the art would be able to readily ascertain the functional binding activity of integrins and their cognate binding partners based upon the assays taught in the specification.

Applicants' arguments have been fully considered but not deemed persuasive. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to osteopontin derived peptide comprising amino acids of various SEQ ID NOs wherein the peptide increases cell attachment to a biomaterial and increases cell spread, wherein the peptide binds to at least one receptor on a cell surface, wherein the receptor is an integrin. As was stated in the last Office Action, the specification teaches that SEQ ID NO:11 (elected species) is a an osteopontin-derived fragment with cell attachment and/or cell spread activity (page 7, lines 23-27 and page 8, lines 11-20). The specification teaches that when plates are coated with SEQ ID NO:11, human osteoprogenitor cells attach and spread to the surface. The specification teaches that antibodies to $\alpha_v\beta_3$ integrin significantly diminishes mOC-1016 (SEQ ID NO:15) from binding to human osteoprogenitor cells (page 53, lines 17-21 and

page 54).

The scope sought by Applicant is not supported by an enabling disclosure because the specification fails to teach other cell types which have a SEQ ID NO:11 binding receptor. The instant claims encompass a number of diverse types of cells. The specification fails to teach how one would culture and isolate these very different cells. The specification fails to teach if integrins are found on all of these cells and if there are different receptors that bind osteopontin derived peptides. The specification fails to teach how to differentiate between an integrin receptor and another cell surface molecule. Furthermore, it is not clear if the cell surface molecule that binds SEQ ID NO:11 is an integrin receptor or an "integrin-like receptor" because the specification never disclosed a specific receptor antibody that inhibited SEQ ID NO:11 from binding. There is no predictability as to which integrin receptor (if indeed it is integrin) would bind SEQ ID NO:11. Applicants state that Table 8 illustrates that antibodies to different integrins may be used to block binding to specific integrins, but only antibodies to $\alpha_v\beta_3$ integrin were able to inhibit mOC-1016 (SEQ ID NO:15), *not SEQ ID NO:11*, from binding (table 8, page 54).

Applicants states that it should be noted that one of ordinary skill in the art may identify peptides exhibiting the claimed activities and that peptide size is not critical to binding since the peptide is able to bind when present in the intact full length peptide. This is not found persuasive because the instant specification has failed to teach osteopontin derived peptides with those claimed features (i.e. binds any type of integrin receptor on any type of cell). Furthermore, certain positions in the sequence are critical

to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding/active sites and critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions.

The invention is osteopontin derived peptides with a specific sequence. However, the instant claims encompass that specific sequence and any other sequence outside of that recited sequence (comprising, open language). There is no assurance that sequences outside of the claimed sequence would destroy folding of the peptide and/or affect attachment and binding. Therefore, the instant claims could encompass inoperative polypeptides, which the skilled artisan would not know how to use. Furthermore, the knowledge of one osteopontin derived peptide structure and function does not provide predictability about function of another osteopontin derived peptide. Thus, human osteoprogenitor cells attach and spread to surfaces coated with SEQ ID NOs:9-15 (page 53, line 22-page 54, line 2) and antibodies to $\alpha_v\beta_3$ integrin significantly diminish SEQ ID NO:15 from binding (means SEQ ID NO:15 binds the $\alpha_v\beta_3$ integrin receptor). But this is not tantamount to SEQ ID NO:11 (or any other osteopontin derived peptide) binding any integrin on any cell type. This is demonstrated by the fact that SEQ ID NO:15 was still able to cause human osteoprogenitor cells to attach and spread in the presence of antibodies against CD44 and $\alpha\beta1$ (page 54).

For the reasons discussed above, which include the unpredictability of protein/fragment folding, lack of working examples, direction in the specification and the quantity of experimentation to demonstrate the claimed functions with diverse cell

surface receptors on various cell types and the breadth of the claims which fail to recite any receptor or cell limitations requirements, it would require undue experimentation to use the invention commensurate in scope with the claims. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 112, second paragraph

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is drawn to an osteopontin-derived peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs 7-15, wherein the peptide sequence is not full length human osteopontin.

The instant claims are indefinite because the structural limitation cannot be established. The instant claim encompasses open language (sequences comprising *at least* those specific amino acids listed for each SEQ ID NO:). However, the claim also recites the limitation "wherein the peptide sequence is not full length human osteopontin". The metes and bounds of the instant claim cannot be determined. The instant claim should either be open (comprising *at least* those amino acids listed for the SEQ ID NOs and/or any other sequence that falls on either side) or closed language (consisting only of those amino acids listed for the SEQ ID NOs).

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RMD
February 4, 2004

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